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Analysis of the Clinical Predictive Value of the Novel Inflammatory Indices SII, SIRI, MHR and NHR in Patients with Acute Myocardial Infarction and Their Extent of Coronary Artery Disease

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Background: This study aims to observe the relationship between novel inflammatory markers and AMI, and analyze its correlation with the degree of coronary artery disease.

Methods: Clinical data were collected from the control (510 cases) and AMI (406 cases) groups. The AMI group was classified into mild, moderate and severe according to the Gensini score. Correlation of SII, SIRI, MHR and NHR with Gensini score in AMI patients was analysed using Spearman rank correlation analysis. Factors influencing the degree of coronary lesion in AMI were analysed by multi-factor ordinal logistic regression. The predictive value of the novel inflammatory markers for AMI and its coronary severity was assessed using ROC curves. Risk prediction of the extent of coronary artery disease in AMI using the Nomogram for novel inflammatory indices.

Results: The levels of SII, SIRI, MHR and NHR were significantly higher in the AMI group than in the control group. With increasing Gensini score, all four novel inflammatory indices showed an increasing trend. And four novel inflammatory indices were positively correlated with Gensini scores. Meanwhile, SII, SIRI and MHR were independent risk factors for the extent of coronary artery disease in AMI. SII, SIRI, MHR and NHR have good predictive value for AMI, and have predictive value for mild and severe AMI, but have no predictive value for moderate AMI. The nomogram results showed that SII, SIRI and MHR had some predictive value for the degree of coronary artery disease in AMI. The nomogram results showed that SII, SIRI and MHR had some predictive value for the degree of coronary artery disease in AMI.

Conclusion: The elevated levels of SIRI, SII, MHR, NHR in AMI patients are independent risk factors for the severity of coronary artery disease in AMI patients, and have predictive value to a certain extent.

Keywords: acute myocardial infarction, systemic inflammatory immune index, systemic inflammatory response index, monocyte-to-high-density lipoprotein ratio, neutrophil-to-high-density lipoprotein ratio, clinical predictive value

Introduction

The progress in medical advancements has led to significant improvements in the treatment outcomes of patients with cardiovascular diseases (CVD); however, globally, CVD-related deaths continue to represent a substantial proportion.[1,2] Research findings indicate that in 2019, non-communicable diseases accounted for 74.3% of the total global mortality, totaling 42.03 million deaths. Among non-communicable diseases, CVD emerged as the leading cause of mortality, with CAD being the predominant form of coronary artery disease.[2] The occurrence and development of CAD is mainly based on atherosclerosis, which mainly causes coronary artery stenosis and obstruction due to atherosclerosis and thrombosis, etc., resulting in patients' morbidity.[3] Acute myocardial infarction (AMI) is an acute and critical event in CAD,

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characterized by sudden onset, severe condition and high risk of death.[4] Although current treatments, such as surgery and thrombectomy, have reduced patient mortality, the outcomes for AMI patients are still less than ideal. Therefore, for the diagnosis, treatment and prognosis of AMI patients, early detection of the patient's condition is of great importance.

Atherosclerosis (AS) represents the foundation and primary risk factor for AMI.[5,6] The accumulation of cholesterol within the inner wall of blood vessels, the formation of foam cells, and the sustained inflammatory response are pivotal processes in the genesis and progression of atherosclerosis.[7,8] Neutrophils, monocytes, platelets, and lymphocytes have been identified as playing pathogenic roles in the inflammatory response, which is a key factor in the pathogenesis of AS.[7,9] Conversely, HDL exerts a protective effect on the occurrence and development of AS and is inversely correlated with the risk of CAD.[9,10] Consequently, a novel biomarker is constructed based on blood cell count and its subtypes (neutrophils, monocytes, platelets, and lymphocytes), HDL, and other hematological detection indicators, which fully reflects the inflammatory response of the body. This biomarker is advantageous in that it is convenient for clinical multidimensional diagnosis of patients and does not increase the economic burden of patients. Consequently, novel inflammatory markers, including the systemic inflammatory response index (SIRI), systemic inflammatory immune index (SII), monocyte-to-high-density lipoprotein ratio (MHR), and neutrophil-to-high-density lipoprotein ratio (NHR), have emerged as valuable tools in the investigation of cardiovascular diseases in recent years.[11–13] SIRI and SII are novel and stable inflammatory markers that can reflect systemic inflammatory response and local immune response of the human body.[14,15] SIRI mainly includes neutrophils, monocytes and lymphocytes, and has been identified as an independent risk factor for major adverse cardiovascular events (MACE) in patients with acute coronary syndrome following interventional therapy.[16,17] SII encompasses three blood cell indices, namely neutrophils, monocytes, and platelets. Elevated SII levels have been linked to an increased risk of coronary heart disease.[18,19] MHR mainly includes monocyte and HDL, which are considered as biomarkers of oxidative stress in inflammatory state, and independent predictors of AMI occurrence and major adverse cardiovascular events.[20,21] NHR, which mainly includes neutrophils and HDL, has been widely reported as an emerging indicator of inflammation and oxidative stress, and has predictive value for long-term mortality and recurrent myocardial infarction in elderly patients with AMI.[22]

The occurrence and development of AMI are closely related to abnormal inflammatory cells and lipid metabolism. Studies have shown that novel inflammatory markers derived from blood cells, such as neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR), are associated with MACE in AMI patients.[23,24] However, in this study, SIRI and SII contained more indicators related to the occurrence and development of AS, while MHR and NHR contained lipid-related indicators, which were more adequate than the single blood cell indicators of NLR and PLR. New inflammatory markers, including SIRI, SII, MHR and NHR, have been found to be closely associated with cardiovascular diseases. Nevertheless, the aforementioned four indicators have not yet been subjected to comprehensive investigation in the context of AMI. Therefore, the objective of this study is to observe the relationship between SIRI, SII, MHR, and NHR and AMI, as well as to analyze the relationship between them and the degree of coronary artery disease. The findings of this study will provide a reference for early clinical diagnosis and treatment of AMI and will also assist in the assessment of the degree of coronary artery disease in patients.

Materials and Methods

Study Population and Data Collection

This retrospective study of 916 specimens was obtained from Xi'an International Medical Centre (1 January 2022 to 31 December 2023), China. The control population consisted of 510 cases from the hospital's health screening center. 406 patients in the AMI (acute myocardial infarction) group were from the hospital's cardiovascular department. The sample size was estimated by using JMP® Trial 18.0.1 software (JMP Statistical Discovery LLC., USA). Considering a 95% (α=0.05) confidence interval, and a 90% (1-β) power to detect a difference of 0.25 units, the calculated sample size is 677. The total sample size of this study was 916, which met the requirement of 90% efficacy. The diagnosis of acute myocardial infarction is mainly based on the Fourth Universal Definition of Myocardial Infarction (2018) and the criteria recommended by the American College of Cardiology guideline.[25,26] Inclusion criteria: AMI was diagnosed; first onset and symptoms within 12h; coronary angiography was performed in all patients. Exclusion criteria: prior coronary artery

bypass grafting or coronary artery stenting; combined with valvular disease, congenital heart disease, pulmonary heart disease, cardiomyopathy, etc.; primary hepatic and renal dysfunction; suffering from severe infections, malignant tumors, rheumatic diseases, etc.; diseases of the blood system; have undergone bone marrow or organ transplantation; long-term use of anticoagulant drugs and other drugs that affect blood test results.

The clinical data of the study subjects were collected, including sex, age, blood routine, blood lipids and other indicators. The Gensini score of each AMI patient was calculated based on the coronary angiography results (the results were obtained from the patients' hospital records). For details of the Gensini score, see a guide for Gensini score calculation.[27] Patients in the AMI group were divided into mild group (Gensini score < 30), moderate group (30 ≤ Gensini score ≤ 60) and severe group (Gensini score > 60) according to the tertiles of Gensini score.

As this study was a retrospective analysis, informed consent from participants could not be obtained, and received an exemption from the hospital ethics committee. This study was approved by Xi'an International Medical Center Hospital Ethics Committee (GJYX-KY-2024-015), and its protocol abided by the principles of the Declaration of Helsinki.

Detection of Blood Markers and Calculation of the Inflammatory Index

Monocytes, lymphocytes, platelets, and neutrophils were measured using a standard automated haematology analyser (which can count and sort different types of cells in the blood) (SYSMEX-XN9000, Japan). Triglycerides, total cholesterol, HDL, LDL and blood glucose (glucose oxidase method) were measured using a blood biochemistry analyser (which allows blood samples to be taken and chemically analysed) (HITACHI-008AS, Japan). Left Ventricular Ejection Fractions (LVEF%) was measured by echocardiography.

The inflammatory index calculation: SII= neutrophil count ($\times 10^9$/L) ×platelet count ($\times 10^9$/L)/lymphocyte count ($\times 10^9$/L); SIRI =neutrophil count ($\times 10^9$/L) × monocyte count ($\times 10^9$/L)/lymphocyte count ($\times 10^9$/L); MHR =monocyte ($\times 10^9$/L)/high-density-lipoprotein cholesterol (mmol/L) ratio; NHR= neutrophil count ($\times 10^9$/L) /high-density-lipoprotein cholesterol (mmol/L) ratio.

Statistical Analysis

SPSS 22.0 and *R 4.3.3* were used for statistical analysis of the study. Mean ± standard deviation ($\bar{x} \pm s$) was used for normally distributed information, interquartile range [M (Q3–Q1)] for non-normally distributed information, and percentages for categorical variables. The independent samples *t*-test was used to compare normally distributed quantitative variables in the two samples. Non-normally distributed quantitative variables in the two samples were compared using two-sample non-parametric tests. One-way-ANOVA was used to compare normally distributed multiple samples and SNK test was used to compare two groups. Non-normally distributed samples were compared using non-parametric tests. Chi-squared test was used to compare rates of categorical variables. Correlations between the four inflammatory indices and Gensini scores were analysed using Spearman rank correlation. The outcome variable of this study was the degree of coronary artery lesions, which was divided into three grades: mild, moderate, and severe, so this study used multi-factor ordinal logistic regression to analyze the influencing factors of the degree of coronary artery lesions. The predictive value of the four inflammatory indices for AMI and the degree of coronary artery disease was analysed using ROC curves. A nomogram was used to generate a predictive model for the extent of AMI coronary lesions using the four inflammatory indices. The accuracy of the nomogram was assessed using calibration curves.

Results

Comparison of Clinical Characteristics

Comparison of Clinical Characteristics and Indicators Between the Control and AMI Groups

As shown in Table 1, the mean age of the control group was 59.19±7.25 years, and the mean age of the AMI group was 60.08±6.94 years. The proportion of males in the control and AMI groups was 65.69% and 64.29%, respectively. There was no significant difference in age and sex between the AMI group and the control group ($P>0.05$). There was no significant difference in PLT, TC, LDL and TG between AMI group and control group ($P>0.05$). Compared with the control group, the total amount of MONO and NEUT in the blood of the AMI group was significantly higher than that of

Table 1 Demographic Data and Clinical Characteristics of Control and AMI Patients [($\bar{x} \pm s$), M (Q3–Q1)]

Characteristics	Control (n=510)	AMI (n=406)	χ^2/ t	P
Age (years)	59.19±7.25	60.08±6.94	1.358	0.175
Male, n (%)	335 (65.69%)	261 (64.29%)	0.094	0.760
Blood routine examination				
MONO (×10^9/L)	0.374±0.12	0.657±0.254	124.564	0.000
LYMP (×10^9/L)	1.828±0.543	1.467±0.700	9.501	0.000
PLT (×10^9/L)	225.361±60.025	212±74.454	0.653	0.419
NEUT (×10^9/L)	3.304±1.145	7.054±3.076	276.166	0.000
Blood lipid				
LDL (mmol/L)	2.613±0.730	2.586±0.770	0.224	0.636
HDL (mmol/L)	1.208±0.312	0.990±0.238	12.531	0.000
TG (mmol/L)	1.34 (0.93,1.92)	1.27 (1.00,1.71)	−0.286	0.775
TC (mmol/L)	4.559±0.909	4.046±0.946	0.030	0.862
Inflammatory index				
SII	391.27 (279.39,531.29)	922.43 (562.78,1647.83)	−13.673	0.000
SIRI	0.62 (0.44,0.91)	2.81 (1.69,5.52)	−16.669	0.000
MHR	0.31 (0.22,0.42)	0.66 (0.47,0.90)	−12.808	0.000
NHR	2.74 (2.04,3.62)	7.79 (5.89,10.13)	−23.796	0.000

Notes: Data are expressed as n (%) for categorical variables and as mean ± standard deviation ($\bar{x} \pm s$) for continuous variables with normal distribution and as M(Q3-Q1) for continuous variables with non-normal distribution.
Abbreviations: AMI, acute myocardial infarction; M(Q3-Q1), median (interquartile range); MONO, Monocyte; LYMP, Lymphocyte; PLT, Platelet; NEUT, Neutrophil; TC, Total cholesterol; LDL, Low-density lipoprotein; TG, Triglyceride; HDL, High density lipoprotein; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; MHR, monocyte-to-high-density lipoprotein ratio; NHR, Neutrophil to-high-density lipoprotein ratio. $P<0.05$ was considered statistically significant.

the control group, and the total amount of LYMP was significantly lower than that of the control group ($P<0.05$). Blood HDL content was significantly lower in the AMI group than in the control group ($P<0.05$). The inflammation index SII, SIRI, MHR and NHR values of the AMI group were significantly higher than those of the control group ($P<0.05$).

Comparison of Clinical Features and Indicators of AMI Patients with Different Gensini Scores

406 patients with AMI were divided into three groups according to the Gensini score. The mean age of the three groups was 61.70±7.56, 63.39±9.23 and 61.64±3.46 years, respectively. The proportion of males in each group was 67.48%, 69.57% and 69.66%, respectively. There was no significant difference in age and sex between the three groups ($P>0.05$). There was no significant difference in the proportions of hypertension and diabetes among the three groups ($P>0.05$). There was no significant difference in heart rate, glucose, PLT, MONO and TG among the three groups ($P>0.05$). Comparison of smoking and Killip (II-IV) ratio among the three groups showed statistically significant differences, and with increasing Gensini score, smoking and Killip (II-IV) ratio showed an increasing trend ($P<0.05$). LVEF%, LYMP, NEUT, LDL, HDL and TC values of the three groups were compared and the differences were statistically significant ($P<0.05$). With increasing Gensini score, LVEF%, LYMP and HDL showed a decreasing trend, whereas NEUT, LDL and TC showed an increasing trend ($P<0.05$). The inflammatory indices SII, SIRI, MHR and NHR of the three groups were compared and the differences were statistically significant, and with the increase in Gensini score the four inflammatory indices showed an upward trend ($P<0.05$, Table 2).

Correlation Analysis of SII, SIRI MHR and NHR with Gensini Score

Spearman correlation analysis of SII, SIRI, MHR and NHR with Gensini scores in AMI patients showed a positive correlation ($P<0.05$) between SII, SIRI, MHR and NHR with Gensini scores in AMI patients. The rank correlation

Table 2 Comparison of Clinical Features of AMI Patients with Different Gensini Scores [($\bar{x} \pm s$), M (Q3–Q1)]

Characteristics	AMI (n=406)			χ^2/ F / Z	P
	Mild group (n=123)	Moderate group (n=138)	Severe group (n=145)		
Male, n (%)	83 (67.48%)	96 (69.57%)	101 (69.66%)	0.182	0.913
Age (years)	61.70±7.56	63.39±9.23	61.64±3.46	2.676	0.070
Hypertension, n (%)	73 (63.41%)	90 (65.22%)	93(64.14%)	1.075	0.584
Diabetes, n (%)	35 (28.46%)	42 (30.43%)	44 (30.34%)	0.154	0.926
Heart rate, times /min	82.78±12.09	84.42±12.40	83.45±12.50	0.586	0.557
Smoking, n (%)	61 (49.59%)	84 (60.87%)	97 (66.90%) [a]	8.414	0.015
Killip (II-IV), n (%)	31 (25.20%)	45 (32.61%)	70 (48.28%) [ab]	16.401	0.000
LVEF%	54.30 ±5.41	52.98±6.84	49.36±7.96 [ab]	18.890	0.000
Glucose (mmol/L)	5.11(4.62,6.15)	5.60 (5.11,8.99)	5.89 (5.09,7.92)	4.062	0.131
Blood routine examination					
MONO ($\times10^9$/L)	0.72±0.25	0.74±0.19	0.75±0.24	0.684	0.505
LYMP ($\times10^9$/L)	1.73±0.58	1.45±0.44[a]	1.33±0.58 [a]	18.948	0.000
PLT ($\times10^9$/L)	206.18±66.07	207.49±40.95	213.97±54.48	0.814	0.444
NEUT ($\times10^9$/L)	6.96±2.75	6.86±2.33	7.65±3.04 [ab]	3.474	0.032
Blood lipid					
LDL (mmol/L)	2.51±0.72	2.50±0.80	2.75±0.88[ab]	4.311	0.014
HDL (mmol/L)	1.01±0.20	0.88±0.19[a]	0.83±0.14[ab]	35.786	0.000
TG (mmol/L)	1.28(0.85,1.74)	1.23(0.88,1.66)	1.31(1.02,1.73)	1.500	0.472
TC (mmol/L)	4.85±0.88	4.96±0.86	5.13±0.89[a]	3.495	0.031
Inflammatory index					
SII	685.77(534.89,1139.90)	976.33(723.86,1416.11) [a]	1148.46(752.11,1921.32) [ab]	37.696	0.000
SIRI	2.46(1.91,4.08)	3.56(2.22,4.98) [a]	4.07(2.57,6.70) [ab]	26.039	0.000
MHR	0.69(0.58,0.85)	0.87(0.68,1.00) [a]	0.87(0.69,1.16) [a]	32.939	0.000
NHR	6.47(4.96,8.72)	7.73(6.21,10.33) [a]	8.38(6.94,11.07) [ab]	32.335	0.000

Note: Data are expressed as n (%) for categorical variables and as mean ± standard deviation ($\bar{x} \pm s$) for continuous variables with normal distribution and as M(Q3-Q1) for continuous variables with non-normal distribution. $P<0.05$ was considered statistically significant. [a]$P<0.05$ compared to the mild group. [b]$P<0.05$ compared the moderate group.

Abbreviations: AMI, acute myocardial infarction; M(Q3-Q1), median (interquartile range); BMI, Body mass index; LVEF, Left Ventricular Ejection Fractions; MONO, Monocyte; LYMP, Lymphocyte; PLT, Platelet; NEUT, Neutrophil; TC, Total cholesterol; LDL, Low-density lipoprotein; TG, Triglyceride; HDL, High density lipoprotein; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; MHR, monocyte-to-high-density lipoprotein ratio; NHR, Neutrophil to-high-density lipoprotein ratio.

coefficients of SII, SIRI, MHR and NHR with Gensini scores were 0.3244, 0.2767, 0.2846 and 0.3146, respectively (Figure 1).

The Factors Influencing the Degree of Coronary Lesion in AMI Were Analyzed by Multi-Factor Ordinal Logistic Regression

The results of the parallelism hypothesis test showed that $P=0.249>0.1$, which was consistent with proportional dominance, ie, the individual regression equations of each model were parallel and satisfied the prerequisites for ordered logistic regression analysis. The influential factors related to the degree of coronary lesion in AMI in univariate analysis were taken as independent variables, and the degree of coronary lesion in AMI was taken as dependent variable and included in the multi-factor ordered classification logistic regression model. The results showed that Killip grade and the new inflammation indicators SII, SIRI and MHR were independent risk factors for the degree of coronary lesion in AMI ($P<0.05$). LVEF% was a protective factor for the degree of coronary lesion in

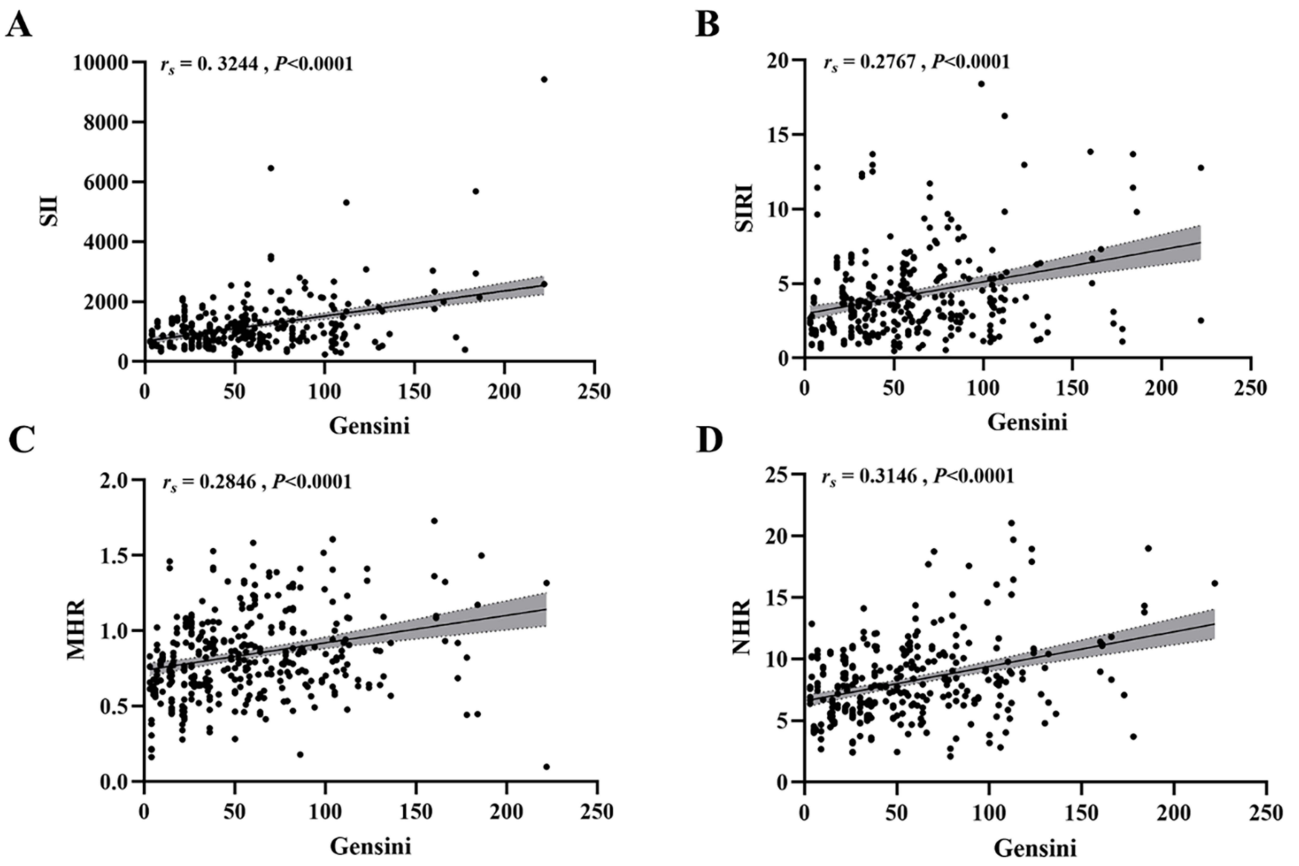

Figure 1 Correlation analysis of SII, SIRI, MHR and NHR with Gensini sore. (**A**) Correlation analysis of SII with Gensini sore; (**B**) Correlation analysis of SIRI with Gensini sore; (**C**) Correlation analysis of MHR with Gensini sore; (**D**) Correlation analysis of NHR with Gensini sore.
Abbreviations: SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; MHR, monocyte-to-high-density lipoprotein ratio; NHR, Neutrophil to-high-density lipoprotein ratio.

AMI (P<0.05). The goodness of fit test results (χ^2=181.46, P=0.005) showed that the model had a good goodness of fit (Table 3).

ROC Curve Analysis

ROC Curve Analysis of SII, SIRI, MHR and NHR for AMI

ROC curve to assess the predictive value of the novel inflammatory indicators SII, SIRI, MHR and NHR for AMI, the results showed that the AUCs of SII, SIRI, MHR and NHR were 0.896, 0.972, 0.952 and 0.957, respectively (P<0.05);

Table 3 Multi-Factor Ordinal Logistic Regression for the Degree of Coronary Lesion in AMI

Indicators	β	Standard Error	Wald χ^2	Odds Ratio	95% CI	*P*
Killip class	0.062	0.021	8.847	1.064	1.021–1.109	0.003
LVEF%	−0.201	0.07	−2.889	0.818	0.713–0.937	0.004
SII	0.001	0.000	25.126	1.001	1.001–1.002	0.000
SIRI	0.305	0.059	8.081	1.357	1.076–2.258	0.008
MHR	2.233	0.494	20.444	9.323	3.510–24.766	0.000
NHR	0.019	0.048	0.166	1.020	0.927–1.121	0.684

Note: P<0.05 was considered statistically significant.
Abbreviations: AMI, acute myocardial infarction; LVEF, Left Ventricular Ejection Fractions; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; MHR, monocyte-to-high-density lipoprotein ratio; NHR, Neutrophil to-high-density lipoprotein ratio; 95% CI, 95% confidence interval.

Table 4 ROC Curve Analysis for AMI

Indicators	Sensitivity (%)	Specificity (%)	Best Cut-Off Point	AUC	95% CI	*P*
SII	83.33	77.61	557.22	0.896	0.876–0.916	0.000
SIRI	91.10	93.12	1.39	0.972	0.962–0.981	0.000
MHR	89.44	91.20	0.53	0.952	0.938–0.966	0.000
NHR	89.94	89.20	4.66	0.957	0.945–0.969	0.000
Comebine	95.64	91.72	0.30	0.984	0.978–0.990	0.000

Abbreviations: AMI, acute myocardial infarction; AUC, Area under the curve; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; MHR, monocyte-to-high-density lipoprotein ratio; NHR, Neutrophil to-high-density lipoprotein ratio; 95% CI, 95% confidence interval.

the optimal cutoffs were 557.22, 1.39, 0.53 and 4.66, respectively ($P<0.05$); and the combined detection of the four inflammation indicators of AUC was 0.984, sensitivity was 95.64% and specificity was 91.72% (Table 4, $P<0.05$). The value of applying the four inflammatory indicators to predict the occurrence of AMI was high (Figure 2, $P<0.05$).

ROC Curve Analysis of SII, SIRI, MHR and NHR for Degree of Coronary Lesions in AMI

The predictive value of the novel inflammatory markers SII, SIRI, MHR and NHR for the degree of AMI was evaluated using ROC curves with the degree of coronary artery disease as the outcome variable. The results of ROC analysis showed that the AUCs of SII, SIRI, MHR and NHR in the mild group were 0.673, 0.642, 0.677 and 0.661, respectively, and the AUCs of the combined test in the mild group were 0.738, with a sensitivity of 78.45% and a specificity of 59.44% ($P<0.05$). The AUC of SII, SIRI, MHR and NHR for the severe group were 0.650, 0.627, 0.609 and 0.638 respectively ($P<0.05$); the AUC of the four inflammation indicators for the severe group was 0.694 ($P<0.05$). The AUC of the four inflammation indicators for the severe group was 0.694, the sensitivity was 46.94% and the specificity was 87.43% ($P<0.05$); SII, SIRI, MHR and NHR had no predictive value for the moderate group ($P>0.05$). The four inflammatory indices had some predictive value for the mild group and the severe group in the degree of coronary lesions in AMI (Table 5 and Figure 3, $P<0.05$).

Risk Prediction of AMI Coronary Lesion Degree

The SII, SIRI, MHR and NHR in the risk factor model for degree of AMI coronary lesions were output as a nomogram (Figure 4) by R Studio software, which allowed prediction of the degree of AMI coronary lesions. The inflammation

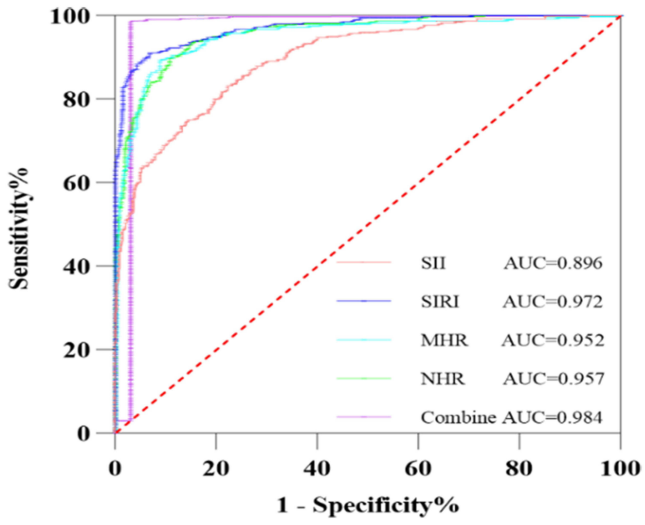

Figure 2 ROC curve analysis for AMI.
Abbreviations: AUC, Area under the curve; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; MHR, monocyte-to-high-density lipoprotein ratio; NHR, Neutrophil to-high-density lipoprotein ratio.

Table 5 ROC Curve Analysis for Degree of Coronary Lesions in AMI

Group	Indicators	Sensitivity (%)	Specificity (%)	Cut-Off Point	AUC	95% CI	*P*
Mild group	SII	48.84	80.61	660.41	0.673	0.619–0.728	0.000
	SIRI	58.51	67.84	2.83	0.642	0.585–0.699	0.000
	MHR	66.74	63.63	0.78	0.677	0.621–0.732	0.000
	NHR	46.33	80.61	6.14	0.661	0.606–0.717	0.000
	Comebine	78.45	59.44	0.263	0.738	0.689–0.788	0.000
Moderate group	SII	76.83	36.64	714.00	0.510	0.452–0.567	0.751
	SIRI	65.23	43.74	2.85	0.503	0.445–0.562	0.910
	MHR	60.92	54.94	0.81	0.555	0.498–0.613	0.069
	NHR	79.31	29.09	6.06	0.511	0.453–0.569	0.721
	Comebine	97.09	16.41	0.28	0.552	0.495–0.610	0.014
Severe group	SII	36.60	91.63	1639.49	0.650	0.592–0.708	0.000
	SIRI	39.33	83.12	5.31	0.627	0.569–0.685	0.000
	MHR	32.42	88.78	1.08	0.609	0.550–0.667	0.000
	NHR	77.94	45.19	6.68	0.638	0.581–0.695	0.000
	Comebine	46.94	87.43	0.455	0.694	0.638–0.750	0.000

Abbreviations: AMI, acute myocardial infarction; AUC, Area under the curve; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; MHR, monocyte-to-high-density lipoprotein ratio; NHR, Neutrophil to-high-density lipoprotein ratio; 95% CI, 95% confidence interval.

indices SII, SIRI and MHR had a high predictive value for the extent of coronary artery disease in AMI, whereas NHR had a low predictive value. The accuracy of the nomogram in predicting the degree of AMI coronary lesions was assessed using calibration curves (Figure 5). The predictive ability of the model was assessed by repeated sampling of the original data 500 times using the bootstrap internal validation method, which showed a mean absolute error of 0.013, and the calibration curve converged to the ideal curve (mean absolute error <0.05). Each variable in the nomogram has a corresponding individual score, and the sum of all individual scores, projected onto the total score axis, is the predicted probability of risk. As shown in Figure 4, the mean absolute error of the calibration curve was less than 0.05, indicating that the nomogram constructed in this study predicted the risk of individual AMI coronary lesion extent with a good fit to the actual observed individual risket al the accuracy of the nomogram was good.

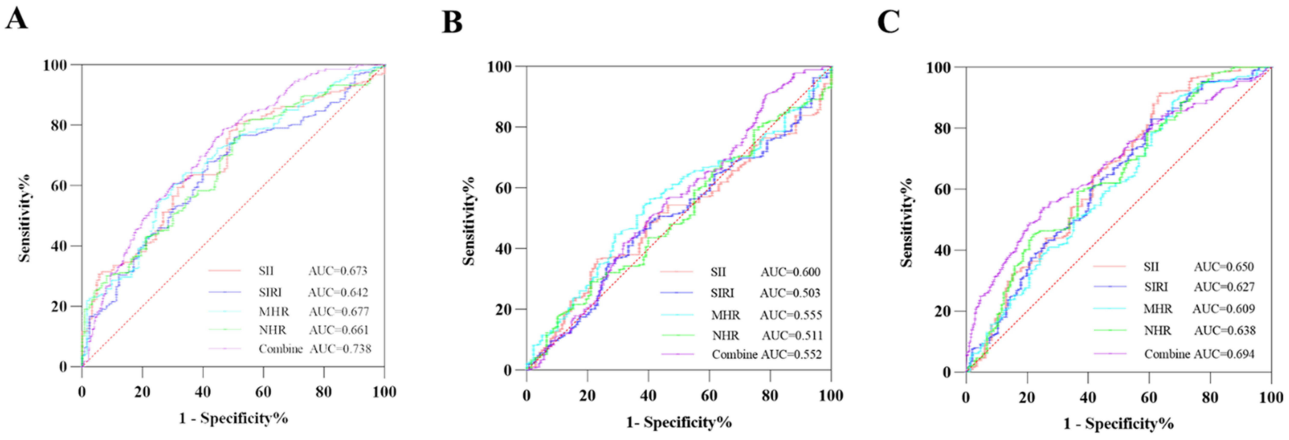

Figure 3 ROC curve for degree of coronary lesions in AMI. (**A**) Mild group; (**B**) Moderate group; (**C**) Severe group.
Abbreviations: AUC, Area under the curve; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; MHR, monocyte-to-high-density lipoprotein ratio; NHR, Neutrophil to-high-density lipoprotein ratio.

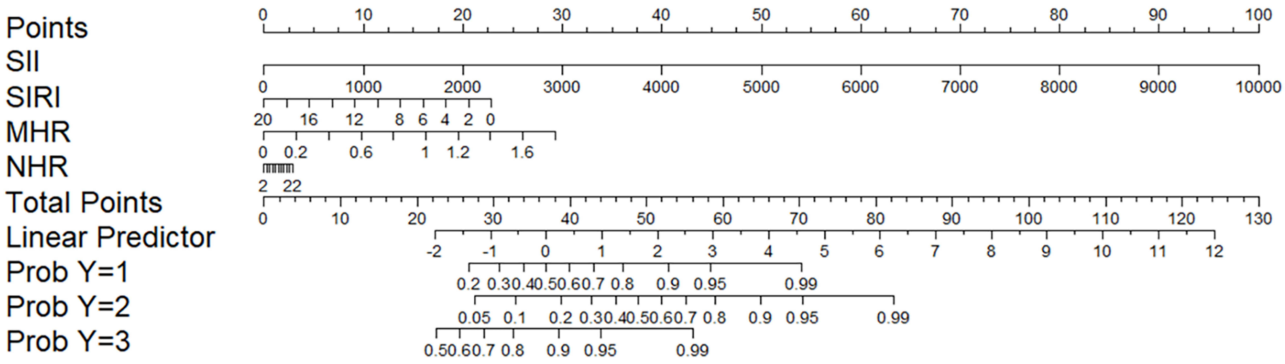

Figure 4 Nomogram for predicting the risk of AMI from coronary lesions. Y=1 represents the group is mild group; Y=2 represents the group is moderate group; Y=3 represents the group is severe group.
Abbreviations: SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; MHR, monocyte-to-high-density lipoprotein ratio; NHR, Neutrophil to-high-density lipoprotein ratio.

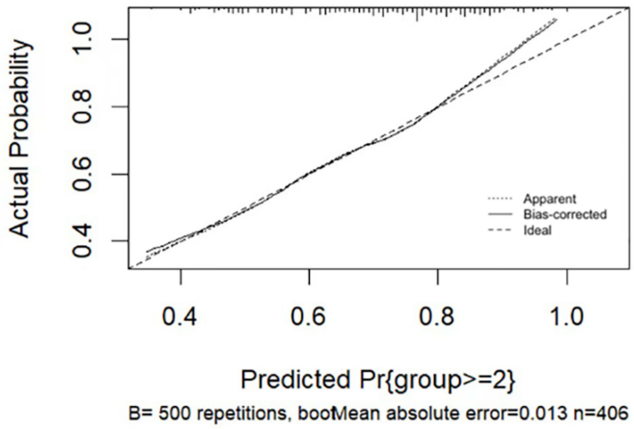

Figure 5 Calibration curves for predicting the extent of coronary lesions in AMI using a nomogram. B=500 repetitions, boot, mean absolute error=0.013, n=406. The mean absolute error is less than 0.05, indicating that the predicted probability of the degree of coronary lesions in AMI in the model is in good agreement with the actual probability.

Discussion

AMI is a form of irreversible myocardial injury that is primarily caused by acute coronary artery infarction. This results in ischemia and hypoxia of distal blood vessels and myocardium, which in turn causes persistent severe retrosternal pain.[4] The continuous ischemia and hypoxia of myocardial tissue can lead to a series of inflammatory reactions, including the infiltration of a large number of inflammatory cells, the release of a large number of inflammatory factors, and the further aggravation of myocardial damage.[28] The results of this study demonstrated that the number of monocytes and neutrophils in the blood of AMI patients was significantly increased in comparison to healthy subjects, while the number of lymphocytes and the level of HDL were significantly decreased. This finding is consistent with previous research.[7,9,29] It is postulated that AMI patients may exhibit an overt inflammatory response, accompanied by a deficiency in anti-inflammatory substances such as HDL.[29]

The pathogenesis of AMI is influenced by the actions of immune cells and inflammatory processes. Studies have demonstrated that the number of white blood cells and the level of C-reactive protein in patients with coronary heart disease are significantly elevated.[30] These factors are associated with the severity of coronary heart disease, the stability of atherosclerotic plaques, and patient mortality.[30] Additionally, higher levels of inflammatory markers are predictive of a higher risk of cardiovascular disease.[31] In patients presenting with chest pain, it is of the utmost importance to assess the severity of coronary artery disease in order to determine the optimal treatment and stratified management of associated disease risk.[32] White blood cells and their classification subgroups (neutrophils, monocytes, lymphocytes,

etc) are accessible clinical test results that can be used to assess the level of inflammation in patients with coronary artery disease,[33] and elevated WBC levels are independent predictors of mortality in AMI patients.[34] Neutrophils represent a significant subgroup of white blood cells and have been demonstrated to play a pivotal role in the body's inflammatory response.[35] Atherosclerosis studies have demonstrated that neutrophils can induce smooth muscle cell dissolution and death, thereby exacerbating inflammation.[36] Furthermore, a considerable number of neutrophils are present in coronary artery diseases,[37] and elevated myeloperoxidase levels of neutrophils may also contribute to the development of coronary atherosclerosis.[38] Monocytes, a unique subset of white blood cells, infiltrate endothelial cells and differentiate into macrophages. These macrophages then phagocytose lipids, forming foam cells. This process results in the release of pro-inflammatory factors, reactive oxygen species, and proteolytic enzymes, which further exacerbate atherosclerotic inflammation.[39,40] Studies have demonstrated a correlation between the number of monocytes in the peripheral blood and the progression of coronary plaques following an AMI. The peak value of these monocytes is the most reliable predictor of plaque progression.[41] Lymphocytes are also an indispensable part of chronic inflammation in atherosclerosis. They can infiltrate into ischemic myocaroma and induce monocyte infiltration by secreting interleukin-10. Decreased peripheral blood count is positively correlated with MACE and poor prognosis of patients.[42,43] The platelet content is a crucial indicator in conventional blood cell counts, exhibiting a dual role in atherosclerosis. On the one hand, it accelerates plaque formation through adhesion to the inner wall of blood vessels.[44] On the other hand, it promotes inflammation and thrombosis.[44,45] Furthermore, it is evident that aberrant lipid metabolism plays a pivotal role in the etiology of AMI. A significant proportion of patients with coronary heart disease are found to be primarily affected by abnormal blood lipid levels, among these, HDL is observed to play an antagonistic role in atherosclerosis, as evidenced by studies.[46] All of the aforementioned indicators play a significant role in the diagnosis of CAD, yet their individual contributions are not without limitations. In recent years, the concept of new inflammatory markers based on blood cell subsets and lipids has provided a new and more comprehensive research direction for medical researchers. SIRI and SII are primarily based on blood cell subsets, while MHR and NHR are based on blood cell subsets and lipids. The results of this study demonstrated that the levels of SIRI, SII, MHR, and NHR in patients with AMI were significantly higher than those in healthy subjects. The results indicated that AMI patients were in a state of obvious inflammation, which was consistent with previous reports.[14,20,22] The results of the ROC curve analysis demonstrated that the AUC values for SII, SIRI, MHR, and NHR were 0.896, 0.972, 0.952, and 0.957, respectively ($P < 0.05$). The optimal critical values were determined to be 557.22, 1.39, 0.53, and 4.66, respectively. The area under the curve (AUC) of the four inflammatory indexes was 0.984, with a sensitivity of 95.64% and a specificity of 91.72%. It is proposed that SII, SIRI, MHR and NHR may be inflammatory markers of AMI and have high predictive value for the occurrence of AMI. In particular, the prediction ability of the four combined tests is obviously better than that of the four independent tests.

The Gensini score is an efficacious index for the evaluation of the extent of coronary artery disease.[47] The use of varying weight coefficients based on the severity of coronary artery branches allows for a more objective and comprehensive reflection of the disease's severity.[47,48] Accordingly, in this study, AMI patients were divided into three groups based on their Gensini scores: mild, moderate, and severe. The study then observed and compared the differences in general clinical data and SIRI, SII, MHR, and NHR between the three groups. The results demonstrated a downward trend in LVEF%, LYMP and HDL with increasing Gensini score, while NEUT, LDL and TC exhibited an upward trend. Concomitantly, the levels of SII, SIRI, MHR, and NHR exhibited an upward trend. It can be postulated that as the severity of coronary artery disease increases, the prevalence of abnormal blood lipid metabolism in AMI patients becomes more pronounced, accompanied by elevated levels of inflammation.

Previous studies have demonstrated that SII is a risk factor for CHD and its severity, and that it is positively correlated with the severity of stable CHD patients using the SYNTAX score.[19,49] In a study conducted by Jin et al, 85,000 respondents were observed for a period of 10 years, the results demonstrated that in patients under the age of 60, an increased SIRI was positively correlated with a higher incidence of acute coronary syndrome.[50] In addition, MHR and NHR are also associated with the risk of cardiovascular disease.[51,52] The results of the multi-factor ordered logistic regression analysis indicated that Killip grade, SII, SIRI, and MHR were independent risk factors for the degree of coronary artery disease in AMI. NHR has not been demonstrated to be an independent risk factor for the degree of coronary artery disease in AMI, potentially due to the fact that neutrophils are not a significant factor in the

formation of atherosclerosis, while monocytes are a major cell in the formation of AS and a predictor of the occurrence of coronary artery disease.[53,54] ROC was employed to assess the predictive value of novel inflammatory markers on AMI lesion severity. The results demonstrated that the AUC of SII, SIRI, MHR, and NHR in the mild group were 0.673, 0.642, 0.677, and 0.661, respectively. Additionally, the AUC of the combined detection of the four indicators in the mild group was 0.738. The sensitivity and specificity were 78.45% and 59.44%, respectively. The AUC of SII, SIRI, MHR, and NHR in the severe group were 0.650, 0.627, 0.609, and 0.638, respectively ($P < 0.05$). The AUC of the four inflammatory indexes was 0.694, with a sensitivity of 46.94% and a specificity of 87.43% ($P < 0.05$). The SII, SIRI, MHR, and NHR did not demonstrate predictive value for the moderate group. Furthermore, Spearman correlation analysis demonstrated a positive correlation between the levels of SII, SIRI, MHR, and NHR in AMI patients and Gensini scores. It is proposed that SII, SIRI, MHR, and NHR may be useful in predicting the extent of coronary artery disease in AMI patients. The higher the SII, SIRI, MHR, and NHR, the more severe the coronary artery disease in AMI patients may be. This can provide a reference for clinicians to judge the condition of patients as early as possible.

The nomogram model, which is based on the core diagnostic indicators, can be utilized for the purpose of patient risk assessment and the early diagnosis of disease. The nomogram model has been utilized in the context of a diverse array of diseases, including pregnancy-induced hypertension,[55] early-stage diabetic nephropathy,[56] and coronary artery disease.[57] In this study, the risk factor model of AMI coronary artery disease degree was output into a column graph by R Studio software, which enabled the degree of AMI coronary artery disease to be predicted. The SII, SIRI, and MHR were found to be effective in predicting the degree of coronary artery disease in AMI, while the NHR was found to be less effective in this regard. Calibration curves were employed to assess the precision of the nomogram in forecasting the severity of coronary artery disease in AMI. A re-sampling method was employed to conduct 500 iterations of the original data set, thereby enabling an assessment of the model's predictive capabilities. The results demonstrated that the mean absolute error was 0.013, and the calibration curve converged to the ideal curve (mean absolute error <0.05). Each variable in the column chart is assigned a corresponding individual score, and the sum of all individual scores is projected onto the total score axis, which represents the predicted risk probability. The mean absolute error of the calibration curve was less than 0.05, indicating that the nomogram constructed in this study for predicting the risk of coronary artery lesions in individuals with AMI is an accurate representation of the actual observed individual risk.

In conclusion, the elevated levels of novel inflammatory markers SIRI, SII, MHR, and NHR in AMI patients are positively correlated with the degree of coronary artery disease, which is an independent risk factor for the severity of coronary artery disease in AMI patients and has predictive value to a certain extent. This provides a reference for the early clinical diagnosis and treatment of AMI, as well as for the assessment of the degree of coronary artery disease. Concurrently, the nomogram model proposed in this study exhibits satisfactory predictive capacity, thereby offering a reference for early clinical estimation of the degree of coronary artery disease in AMI patients. It should be noted that this study is not without limitations. The four inflammatory indicators demonstrated no predictive value in the moderate group, which may be attributed to differences in sample size, study design, overall selection, statistical methods, and outcome measurement. In addition, this study did not include SYNTAX score and did not distinguish NSTEMI from STEMI, which limited the comprehensiveness of the conclusions of this study. In the future, we will also expand the sample size and improve the research methods in order to provide a more comprehensive reference for clinical diagnosis and treatment of AMI. Furthermore, the retrospective nature of the study and single center study limit the persuasiveness of the results. Additionally, the dynamic changes of various indicators could not be comprehensively observed.

Author Contributions

Hui Sun and Haiying Liu share first authorship. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no conflict of interest.

References

1. GBD 2021 Diabetes Collaborators. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet*. 2023;402(10397):203–234. doi:10.1016/S0140-6736(23)01301-6
2. Bai J, Cui J, Shi F, Yu C. Global epidemiological patterns in the burden of main non-communicable diseases, 1990-2019: relationships with socio-demographic index. *Int J Public Health*. 2023;68:1605502. doi:10.3389/ijph.2023.1605502
3. Sutton NR, Banerjee S, Cooper MM, et al. Coronary artery disease evaluation and management considerations for high risk occupations: commercial vehicle drivers and pilots. *Circ Cardiovasc Interv*. 2021;14(6):e009950. doi:10.1161/CIRCINTERVENTIONS.120.009950
4. Frampton J, Ortengren AR, Zeitler EP. Arrhythmias after acute myocardial infarction. *Yale J Biol Med*. 2023;96(1):83–94. doi:10.59249/LSWK8578
5. Wang H, Eitzman DT. Acute myocardial infarction leads to acceleration of atherosclerosis. *Atherosclerosis*. 2013;229(1):18–22. doi:10.1016/j.atherosclerosis.2013.04.004
6. Katz AE, Gupte T, Ganesh SK. From atherosclerosis to spontaneous coronary artery dissection: defining a clinical and genetic risk spectrum for myocardial infarction. *Curr Atheroscler Rep*. 2024;26(7):331–340. doi:10.1007/s11883-024-01208-4
7. Murad HAS, Rafeeq MM, Alqurashi TMA. Role and implications of the CXCL12/CXCR4/CXCR7 axis in atherosclerosis: still a debate. *Ann Med*. 2021;53(1):1598–1612. doi:10.1080/07853890.2021.1974084
8. Bäck M, Yurdagul A, Tabas I, Öörni K, Kovanen PT. Inflammation and its resolution in atherosclerosis: mediators and therapeutic opportunities. *Nat Rev Cardiol*. 2019;16(7):389–406. doi:10.1038/s41569-019-0169-2
9. Murphy AJ, Woollard KJ, Suhartoyo A, et al. Neutrophil activation is attenuated by high-density lipoprotein and apolipoprotein A-I in in vitro and in vivo models of inflammation. *Arterioscler Thromb Vasc Biol*. 2011;31(6):1333–1341. doi:10.1161/ATVBAHA.111.226258
10. Choi HY, Iatan I, Ruel I, et al. Docetaxel as a model compound to promote HDL (high-density lipoprotein) biogenesis and reduce atherosclerosis. *Arterioscler Thromb Vasc Biol*. 2023;43(5):609–617. doi:10.1161/ATVBAHA.122.318275
11. Dong W, Gong Y, Zhao J, Wang Y, Li B, Yang Y. A combined analysis of TyG index, SII index, and SIRI index: positive association with CHD risk and coronary atherosclerosis severity in patients with NAFLD. *Front Endocrinol*. 2024;14:1281839. doi:10.3389/fendo.2023.1281839
12. Song Y, Zhao Y, Shu Y, et al. Combination model of neutrophil to high-density lipoprotein ratio and system inflammation response index is more valuable for predicting peripheral arterial disease in type 2 diabetic patients: a cross-sectional study. *Front Endocrinol*. 2023;14:1100453. doi:10.3389/fendo.2023.1100453
13. Lamichhane P, Agrawal A, Abouainain Y, Abousahle S, Regmi PR. Utility of neutrophil-to-high-density lipoprotein-cholesterol ratio in patients with coronary artery disease: a narrative review. *J Int Med Res*. 2023;51(4):3000605231166518. doi:10.1177/03000605231166518
14. Zhang D, Zeng Y, Sun B, et al. Inflammatory indices-systemic immune-inflammation index (SII) and systemic inflammatory response index (SIRI)-during pregnancy and associations with gestational diabetes mellitus. *J Inflamm Res*. 2024;17:6521–6532. doi:10.2147/JIR.S474154
15. Wang RH, Wen WX, Jiang ZP, et al. The clinical value of neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), platelet-to-lymphocyte ratio (PLR) and systemic inflammation response index (SIRI) for predicting the occurrence and severity of pneumonia in patients with intracerebral hemorrhage. *Front Immunol*. 2023;14:1115031. doi:10.3389/fimmu.2023.1115031
16. Li Q, Ma X, Shao Q, et al. Prognostic impact of multiple lymphocyte-based inflammatory indices in acute coronary syndrome patients. *Front Cardiovasc Med*. 2022;9:811790. doi:10.3389/fcvm.2022.811790
17. Han K, Shi D, Yang L, et al. Prognostic value of systemic inflammatory response index in patients with acute coronary syndrome undergoing percutaneous coronary intervention. *Ann Med*. 2022;54(1):1667–1677. doi:10.1080/07853890.2022.2083671
18. Karadeniz FÖ, Karadeniz Y, Altuntaş E. Systemic immune-inflammation index, and neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios can predict clinical outcomes in patients with acute coronary syndrome. *Cardiovasc J Afr*. 2023;34:1–7. doi:10.5830/CVJA-2023-011
19. Candemir M, Kiziltunç E, Nurkoç S, Şahinarslan A. Relationship between systemic immune-inflammation index (SII) and the severity of stable coronary artery disease. *Angiology*. 2021;72(6):575–581. doi:10.1177/0003319720987743
20. Cao J, Li R, He T, Zhang L, Liu H, Wu X. Role of combined use of mean platelet volume-to-lymphocyte ratio and monocyte to high-density lipoprotein cholesterol ratio in predicting patients with acute myocardial infarction. *J Cardiothorac Surg*. 2023;18(1):172. doi:10.1186/s13019-023-02268-4
21. Zhang Y, Li S, Guo YL, et al. Is monocyte to HDL ratio superior to monocyte count in predicting the cardiovascular outcomes: evidence from a large cohort of Chinese patients undergoing coronary angiography. *Ann Med*. 2016;48(5):305–312. doi:10.3109/07853890.2016.1168935
22. Huang JB, Chen YS, Ji HY, et al. Neutrophil to high-density lipoprotein ratio has a superior prognostic value in elderly patients with acute myocardial infarction: a comparison study. *Lipids Health Dis*. 2020;19(1):59. doi:10.1186/s12944-020-01238-2
23. Wang H, Li L, Ma Y. Platelet-to-lymphocyte ratio a potential prognosticator in acute myocardial infarction: a prospective longitudinal study. *Clin Cardiol*. 2023;46(6):632–638. doi:10.1002/clc.24002
24. Li X, Yu C, Liu X, et al. A prediction model based on systemic immune-inflammatory index combined with other predictors for major adverse cardiovascular events in acute myocardial infarction patients. *J Inflamm Res*. 2024;17:1211–1225. doi:10.2147/JIR.S443153
25. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth Universal Definition of Myocardial Infarction(2018). *J Am Coll Cardiol*. 2018;72(18):2231–2264. doi:10.1016/j.jacc.2018.08.1038
26. Emergency Physician Branch of Chinese Medical Doctor Association, Emergency Medicine Expert Committee of Capacity Building and Continuing Education Center of National Health Commission, Emergency and First Aid Branch of China Medical Care International Exchange Promotion Association. Guidelines for rapid emergency diagnosis and treatment of acute coronary syndrome (2019). *Chin J Emerg Med*. 2019;28(4):421–428. Chinese.

27. Rampidis GP, Benetos G, Benz DC, Giannopoulos AA, Buechel RR. A guide for gensini score calculation. *Atherosclerosis*. 2019;287:181–183. doi:10.1016/j.atherosclerosis.2019.05.012
28. Ong SB, Hernández-Reséndiz S, Crespo-Avilan GE, et al. Inflammation following acute myocardial infarction: multiple players, dynamic roles, and novel therapeutic opportunities. *Pharmacol Ther*. 2018;186:73–87. doi:10.1016/j.pharmthera.2018.01.001
29. Ossoli A, Pavanello C, Giorgio E, Calabresi L, Gomaraschi M. Dysfunctional HDL as a therapeutic target for atherosclerosis prevention. *Curr Med Chem*. 2019;26(9):1610–1630. doi:10.2174/0929867325666180316115726
30. Montecucco F, Liberale L, Bonaventura A, Vecchiè A, Dallegri F, Carbone F. The role of inflammation in cardiovascular outcome. *Curr Atheroscler Rep*. 2017;19(3):11. doi:10.1007/s11883-017-0646-1
31. Silveira Rossi JL, Barbalho SM, Reverete de Araujo R, Bechara MD, Sloan KP, Sloan LA. Metabolic syndrome and cardiovascular diseases: going beyond traditional risk factors. *Diabetes Metab Res Rev*. 2022;38(3):e3502. doi:10.1002/dmrr.3502
32. Mor-Avi V, Patel MB, Maffessanti F, et al. Fusion of three-dimensional echocardiographic regional myocardial strain with cardiac computed tomography for noninvasive evaluation of the hemodynamic impact of coronary stenosis in patients with chest pain. *J Am Soc Echocardiogr*. 2018;31(6):664–673. doi:10.1016/j.echo.2018.01.019
33. Henein MY, Vancheri S, Longo G, Vancheri F. The role of inflammation in cardiovascular disease. *Int J Mol Sci*. 2022;23(21):12906. doi:10.3390/ijms232112906
34. Horne BD, Anderson JL, John JM, et al. Which white blood cell subtypes predict increased cardiovascular risk? *J Am Coll Cardiol*. 2005;45(10):1638–1643. doi:10.1016/j.jacc.2005.02.054
35. Luo J, Thomassen JQ, Nordestgaard BG, Tybjærg-Hansen A, Frikke-Schmidt R. Neutrophil counts and cardiovascular disease. *Eur Heart J*. 2023;44(47):4953–4964. doi:10.1093/eurheartj/ehad649
36. Fernández-Ruiz I. Neutrophil-driven SMC death destabilizes atherosclerotic plaques. *Nat Rev Cardiol*. 2019;16(8):455. doi:10.1038/s41569-019-0214-1
37. Soehnlein O, Weber C. Myeloid cells in atherosclerosis: initiators and decision shapers. *Semin Immunopathol*. 2009;31(1):35–47. doi:10.1007/s00281-009-0141-z
38. Wang XS, Kim HB, Szuchman-Sapir A, McMahon A, Dennis JM, Witting PK. Neutrophils recruited to the myocardium after acute experimental myocardial infarct generate hypochlorous acid that oxidizes cardiac myoglobin. *Arch Biochem Biophys*. 2016;612:103–114. doi:10.1016/j.abb.2016.10.013
39. Gratchev A, Sobenin I, Orekhov A, Kzhyshkowska J. Monocytes as a diagnostic marker of cardiovascular diseases. *Immunobiology*. 2012;217(5):476–482. doi:10.1016/j.imbio.2012.01.008
40. Wu MY, Li CJ, Hou MF, Chu PY. New insights into the role of inflammation in the pathogenesis of atherosclerosis. *Int J Mol Sci*. 2017;18(10):2034. doi:10.3390/ijms18102034
41. Nozawa N, Hibi K, Endo M, et al. Association between circulating monocytes and coronary plaque progression in patients with acute myocardial infarction. *Circ J*. 2010;74(7):1384–1391. doi:10.1253/circj.CJ-09-0779
42. Ley K, Miller YI, Hedrick CC. Monocyte and macrophage dynamics during atherogenesis. *Arterioscler Thromb Vasc Biol*. 2011;31(7):1506–1516. doi:10.1161/ATVBAHA.110.221127
43. Núñez J, Núñez E, Bodí V, et al. Low lymphocyte count in acute phase of ST-segment elevation myocardial infarction predicts long-term recurrent myocardial infarction. *Coron Artery Dis*. 2010;21(1):1–7. doi:10.1097/MCA.0b013e328332ee15
44. Pafili K, Penlioglou T, Mikhailidis DP, Papanas N. Mean platelet volume and coronary artery disease. *Curr Opin Cardiol*. 2019;34(4):390–398. doi:10.1097/HCO.0000000000000624
45. Pasalic L, Wang SS, Chen VM. Platelets as biomarkers of coronary artery disease. *Semin Thromb Hemost*. 2016;42(3):223–233. doi:10.1055/s-0036-1572328
46. Song Y, Yang Y, Zhang J, et al. The apoB100/apoAI ratio is independently associated with the severity of coronary heart disease: a cross sectional study in patients undergoing coronary angiography. *Lipids Health Dis*. 2015;14:150. doi:10.1186/s12944-015-0155-6
47. Işcanlı MD, Metin Aksu N, Evranos B, Aytemir K, Özmen MM. Comparison of TIMI and Gensini score in patients admitted to the emergency department with chest pain, who underwent coronary angiography. *Med Sci Monit*. 2014;20:343–349. doi:10.12659/MSM.889600
48. Zeller T, Seiffert M, Müller C, et al. Genome-wide association analysis for severity of coronary artery disease using the gensini scoring system. *Front Cardiovasc Med*. 2017;4:57. doi:10.3389/fcvm.2017.00057
49. Liu Y, Ye T, Chen L, et al. Systemic immune-inflammation index predicts the severity of coronary stenosis in patients with coronary heart disease. *Coron Artery Dis*. 2021;32(8):715–720. doi:10.1097/MCA.0000000000001037
50. Jin Z, Wu Q, Chen S, et al. The associations of two novel inflammation indexes, sii and siri with the risks for cardiovascular diseases and all-cause mortality: a ten-year follow-up study in 85,154 individuals. *J Inflamm Res*. 2021;14:131–140. doi:10.2147/JIR.S283835
51. Haybar H, Pezeshki SMS, Saki N. Evaluation of complete blood count parameters in cardiovascular diseases: an early indicator of prognosis? *Exp Mol Pathol*. 2019;110:104267. doi:10.1016/j.yexmp.2019.104267
52. Pan X, Zhang X, Ban J, Yue L, Ren L, Chen S. Association of neutrophil to high-density lipoprotein cholesterol ratio with cardiac ultrasound parameters and cardiovascular risk: a cross-sectional study based on healthy populations. *J Inflamm Res*. 2023;16:1853–1865. doi:10.2147/JIR.S406102
53. Dziedzic EA, Gąsior JS, Tuzimek A, et al. Investigation of the associations of novel inflammatory biomarkers-systemic inflammatory Index (SII) and systemic inflammatory response index (siri)-with the severity of coronary artery disease and acute coronary syndrome occurrence. *Int J Mol Sci*. 2022;23(17):9553. doi:10.3390/ijms23179553
54. Peet C, Ivetic A, Bromage DI, Shah AM. Cardiac monocytes and macrophages after myocardial infarction. *Cardiovasc Res*. 2020;116(6):1101–1112. doi:10.1093/cvr/cvz336
55. Zhang P, Zhong X. Analysis of risk factors and construction of nomograph model for critical condition of patients with hypertension during pregnancy. *BMC Pregnancy Childbirth*. 2023;23(1):576. doi:10.1186/s12884-023-05860-7
56. Ding S, Yang Y, Zheng Y, et al. Diagnostic value of the combined measurement of serum HCY and NRG4 in type 2 diabetes mellitus with early complicating diabetic nephropathy. *J Pers Med*. 2023;13(3):556. doi:10.3390/jpm13030556
57. Naoum C, Berman DS, Ahmadi A, et al. Predictive value of age- and sex-specific nomograms of global plaque burden on coronary computed tomography angiography for major cardiac events. *Circ Cardiovasc Imaging*. 2017;10(3):e004896. doi:10.1161/CIRCIMAGING.116.004896